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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/564,148	11/09/2006	Malgorzata Konieczna	PB60333USw	6122

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EXAMINER	
VU, JAKE MINH	

ART UNIT	PAPER NUMBER
1618	

NOTIFICATION DATE	DELIVERY MODE
09/05/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/564,148	KONIECZNA ET AL.	
	Examiner	Art Unit	
	JAKE M. VU	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11 and 15-17* is/are pending in the application.

4a) Of the above claim(s) *15-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/10/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of Applicant's Restriction Requirement Response filed on 06/27/2008; and Information Disclosure Statement filed on 01/10/2006.

- Claims 12-14 have been cancelled.
- Claims 1-11 and 15-17 are pending in the instant application.
- Claims 15-17 are withdrawn from consideration.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Election/Restrictions

Applicant's election with traverse of Group I (claims 1-11) in the reply filed on 06/27/2008 is acknowledged. The traversal is on the ground(s) that MITRA's starch used in Example 10 must be water soluble starch, since this is an essential feature of the invention in MITRA. This is not found persuasive, because soluble glucose polymers have a molecular weight of 500 to 3600 and MITRA disclosed using starch with molecular weights up to 160,000, which is insoluble. Additionally, The European Pharmacopoeia cited in the present application sates on page 1438 that "pregelatinised starch is starch...that has been mechanically processed in the presence of water…to rupture all or part of the starch granules…it contains no added substances but it may be modified to render it compressible and to improve its flow characteristics. The Hand

Book of Pharmaceutical Excipients disclosed pregelatinized starch and starch with the same CAS Registry number of 9005-25-8, have the same molecular weight, and both are used for the same purposes of pharmaceutical tablet formulation, such as a diluent, disintegrant and binder.

Applicant argues that RUSKAY is directed to making a bulking agent in oil-based food and MITRA is directed to stabilized pharmaceutical preparations; thus, there is no motivation to combine the two references. The Examiner finds this argument unpersuasive, because RUSKY is not a reference used in a §103 rejection where motivation to combine is required, instead RUSKY is used as evidence that microcrystalline cellulose, which are powder, inherently has a mean particle size of less than 100um. Additionally, MITRA disclosed using Avicel® PH 102 and 112 (see Table 1), which has a particle size of 100um.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-11 are rejected under 35 U.S.C. 102(b) as being anticipated by MITRA et al (US 5,955,105) as evidenced by HANDBOOK (Handbook of Pharmaceutical

Excipients: 5th edition. pg. 134, 725 and 731 (2006)) and MSDS (Material Safety Data Sheet: L-Thyroxine, sodium salt).

Applicant's claims are directed to a composition comprising of: levothyroxine sodium pentahydrate; 60-85% of microcrystalline cellulose, with a particle size less than or equal to 100um; 5-30% of pregelatinized starch; and lubricants, such as magnesium stearate, wherein the composition is in a form of a tablet.

MITRA teaches a composition comprised of: levothyroxine sodium (see col. 8, Example 10); 80-95% of microcrystalline cellulose (see col. 8, Example 10), such as Avicel® PH 102 (see col. 10, Table 1); 0-15% of starch; and lubricants, such as magnesium stearate (see col. 8, Example 10), wherein the composition is in a form of a tablet (see col. 7, line 28).

MITRA does not disclosed the microcrystalline cellulose has a particle size less than or equal to 100um, or that the levothyroxine sodium is a pentahydrate, or that the starch is pregelatinized.

HANDBOOK disclosed that microcrystalline cellulose, such as Avicel® PH 102, has a mean particle size of 100um (see pg. 134, Table III). Additionally, pregelatinized starch and starch are synonymous with each other, in which both have the same CAS registry number, empirical formula and structural formula.

MSDS disclosed L-thyroxine is synonymous with levothyroxine sodium and has 5H20 in the chemical formula, which is a pentahydrate (see pg. 1 under Synonym and Chemical Formula).

Note, MITRA's composition would inherently have the same stability limitation as claim by Applicant, since MITRA's composition has the same ingredients as claimed by Applicant.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over MITRA et al (US 5,955,105) as evidenced by HANDBOOK (Handbook of Pharmaceutical Excipients: 5th edition. pg. 134, 725 and 731 (2006)) and MSDS (Material Safety Data Sheet: L-Thyroxine, sodium salt) in view of EUROPEAN (European Pharmacopoeia (2002) pg. 1438) and FRANZ et al (US 2003/0032675).

As discussed above, MITRA teaches a composition comprised of: levothyroxine sodium (see col. 8, Example 10); 80-95% of microcrystalline cellulose (see col. 8, Example 10), such as Avicel® PH 102 (see col. 10, Table 1); 0-15% of starch; and lubricants, such as magnesium stearate (see col. 8, Example 10), wherein the composition is in a form of a tablet (see col. 7, line 28). Additional disclosure includes: a tabletting machine is used to compress the resulting dry mixture into tablets (see col. 7, line 27-28)

MITRA does not disclosed the microcrystalline cellulose has a particle size less than or equal to 100um, or that the levothyroxine sodium is a pentahydrate, or that the starch is pregelatinized.

HANDBOOK disclosed that microcrystalline cellulose, such as Avicel® PH 102, has a mean particle size of 100um (see pg. 134, Table III). Additionally, pregelatinized starch and starch are synonymous with each other, in which both have the same CAS registry number, empirical formula and structural formula.

MSDS disclosed L-thyroxine is synonymous with levothyroxine sodium and has 5H20 in the chemical formula, which is a pentahydrate (see pg. 1 under Synonym and Chemical Formula).

MITRA does not specifically teach using pregelatinized starch.

EUROPEAN teaches pregelatinized starch is starch that contains no added substances but it is modified mechanically by rupturing part of the starch granules to render it compressible and to improve its flow characteristics.

FRANZ teaches a thyroid drug formulation comprised of levothyroxine sodium, lactose, microcrystalline cellulose, pregelatinized starch, and magnesium stearate (see claim 6).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to incorporate pregelatinized starch in place of the starch in MITRA's composition. The person of ordinary skill in the art would have been motivated to make those modifications, because pregelatinized starch is more compressible and has improved flow characteristics to improve making the tablet by compression, and

reasonably would have expected success because FRANZ had previously made a levothyroxine formulation that uses pregelatinized starch.

Telephonic Inquiries

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JAKE M. VU whose telephone number is (571)272-8148. The examiner can normally be reached on Mon-Tue and Thu-Fri 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jake M. Vu/
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Art Unit 1618